PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.
Dale B. Schenk et al.	Examiner: Steven H. Standley
Application No.: 10/699,517	Technology Center/Art Unit: 1649
Filed: October 31, 2003	APPELLANTS' BRIEF UNDER 37 CFR §41.37
For: PREVENTION AND TREATMENT OF SYNUCLEINOPATHIC DISEASE	

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
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Sir:

Further to the Notice of Appeal mailed on August 14, 2006 for the above-referenced application, Appellants submit this Brief on Appeal.

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1. REAL PARTY IN INTEREST

Elan Pharma International Ltd. and the Regents of the University of California.

2. RELATED APPEALS AND INTERFERENCES

Appeals are also pending in related Application Nos. 09/723,765 and 10/923,471.

3. STATUS OF CLAIMS

Claims 41-46, 48, 51-55, 71-76 and 79-84 are pending an appealed. Claims 1-40, 47, 49, 50, 56-70, 77 and 78 are cancelled.

4. STATUS OF AMENDMENTS

An amendment after final is being filed herewith canceling withdrawn claims, correcting errors in punctuation in claims 41, 44, 71 and 74, and correcting dependency of claims 51 and 52, which would otherwise depend from a cancelled claim. None of these corrections affects the merits. The listing of claims in the Appendix and status of claims indicated above assumes this amendment will be entered.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The present claims are generally directed to methods of treating or effecting prophylaxis of Parkinson's disease using an agent that induces an immunogenic response to Aβ, and in some claims, a second immunogenic agent that induces an immunogenic response to alpha synuclein. Aβ forms extracellular aggregates, better known as plaques, the characteristic pathology of Alzheimer's disease. Alpha synuclein forms intracellular aggregates, also known as Lewy bodies, the characteristic pathology of Parkinson's disease. The application provides data that immunization with alpha synuclein generates antibodies to alpha synuclein and thereby reduces aggregates of alpha synuclein in a transgenic animal model of Parkinson's disease (paragraph 170 and Fig. 2). The application also provides data that immunization with Aβ (i.e., the principal peptide associated with Alzheimer's disease), which has previously been demonstrated to generate antibodies to Aβ and thereby reduce aggregates of Aβ in an animal

model of Alzheimer's disease, also reduces aggregates of alpha synuclein (i.e., the principal pathology associated with Parkinson's disease). This reduction was observed in both a combined animal model of Alzheimer's and Parkinson's disease in which both aggregates of Aβ and alpha synuclein were present and a model of Parkinson's disease in which aggregates of alpha synuclein were present without abnormal aggregates of Aβ (specification at paragraph 186 and Figs. 5 and 6). That Aβ immunization can reduce synuclein deposits even in the absence of accumulation of abnormal deposits of Aβ suggests that the claimed methods are useful on Parkinson's patients lacking concomitant Alzheimer's disease.

Four independent claims are on appeal.

Independent claim 41 is directed to a method of therapeutically treating a patient suffering from Parkinson's disease. Such methods are generally described at paragraphs 51 and 137. The method comprise administering to the patient an effective regime of an agent that induces an immunogenic response against Aβ. The rationale for administering Aβ against patients with Parkinson's disease is discussed in paragraph 52 and exemplified in paragraph 186 The agent is Aβ or an immunogenic fragment thereof, or an antibody to Aβ, as described at paragraphs 117-132 of the specification.

Claim 54, which depends from claim 41, specifies that the patient is free of Alzheimer's disease. Claim 81, which also depends from claim 41, specifies that the patient is free of clinical symptoms of a disease characterized by extracellular amyloid deposits. Such patients are described at e.g., paragraph 134 of the specification. The rationale for treating such patients is provided by the example at paragraph 186 as discussed above.

Independent claim 44 is also directed to a method of therapeutically treating a patient suffering from Parkinson's disease. However, claim 44 comprises administering to the patient an effective regime of two agents, as generally described at e.g., paragraphs 51 and 137. One agent induces an immunogenic response against Aβ and is Aβ or an immunogenic fragment thereof or an antibody to Aβ as discussed in connection with claim 41. The other agent induces an immunogenic response against alpha synuclein. This agent is alpha synuclein or an immunogenic fragment thereof or an antibody to alpha synuclein, as described at paragraphs 53-116.

Independent claim 71 is directed to a method of prophylactically treating a patient having a known genetic risk of Parkinson's disease. Such methods are described at e.g., paragraph 133 and 137. The method comprises administering to the patient an effective regime of an agent that induces an immunogenic response to Aβ. The agent is Aβ or an immunogenic fragment thereof, or an antibody to Aβ, as , as described at paragraphs 117-132 of the specification.

Claim 79, which depends from claim 71, specifies that the patient is free of Alzheimer's disease. Claim 80, which depends from claim 79 further specifies that the patient has no risk factors of Alzheimer's disease. Such patients are described at e.g., paragraph 134 of the specification.

Independent claim 74 is also directed to a method of prophylactically treating a patient having a known genetic risk of Parkinson's disease. As in claim 44, claim 77 specifies administering two agents. One agent is Aβ or an immunogenic fragment thereof or an antibody to Aβ. The other agent is alpha synuclein or an immunogenic fragment thereof or an antibody to alpha synuclein as described at paragraphs 53-116.

Claim 84, which depends from claim 74, specifies that the patient is free of clinical symptoms of a disease characterized by extracellular amyloid deposits. Such patients are described at e.g., paragraph 134 of the specification.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

6.1 Whether claims 41-46, 48, 50-55, 71-76 and 78-80 lack enablement under 35 USC 112, first paragraph

6.2 Whether claims 41, 42, 44, 45, 46, 48, 50, 51-55, 71, 72, 74, 75, 76 and 80-84 are anticipated by Jensen, US 2002/0187157 [Jensen, 2002] or Jensen, US2003/000086938 [Jensen, 2003] under 35 USC 102(e).

6.3 Whether claims 41, 43-46, 48, 50-55, 71, 73-76, 78-80 and 80-84 would have been obvious under 103(a) over Jensen, 2002 or Jensen, 2003.

7. ARGUMENT

7.1 Claims 41-46, 48, 50-55, 71-76 and 78-80 do not lack enablement under 35 USC 112, first paragraph

7.1.1 The Examiner's Rationale

The Examiner's rationale is stated in the final rejection of May 15, 2006 and the penultimate office action of October 7, 2005. In brief, the Examiner takes the view based on Stedman's Medical Dictionary that therapeutically treating means remediating or curing disease and that a claim that includes "curing" a disease is not enabled absent an example that an animal can be completely cured. The Examiner likewise takes the view based on Stedman's Medical Dictionary that "prophylactically treating" means preventing disease, and that a claim to prophylactically treating a disease is not enabled absent evidence of an animal in which the entire pathology of the disease is prevented (penultimate office action p. 6, final office action at p. 3).

The final rejection refers only to claims 41-46, 48 and 50-55 in the statement of the rejection. However, because the reference to "prophylactically treating" occurs in claim 71 (and claims depending therefrom) and claim 71 was rejected in the penultimate office action, appellants assume the rejection was intended to be applied to all claims.

Appellants also note that the penultimate office action raised other issues relating to enablement. However, the final office action raises only the issue of "completely curing" or "completely preventing." Thus, only this issue is addressed in the present appeal.

7.1.2 Appellants' Position

The rejection raises a question of law of whether claims to a method of therapeutically treating Parkinson's disease or prophylactically treating Parkinson's disease can be enabled without evidence to show that the methods can achieve a *complete* cure or *complete* prevention of disease. The Examiner acknowledges that the claimed methods can reduce levels of alpha synuclein deposits [the principal pathology of Parkinson's disease] in a transgenic animal of model of Parkinson's disease or a transgenic animal model of combined Alzheimer's and Parkinson's disease (penultimate office action at p. 7, second paragraph). However, the Examiner alleges lack of enablement on the grounds that appellants have not shown the claimed

methods can achieve a complete cure or complete prevention of Parkinson's disease (final office action at p. 3).

Before analysis of relevant case law, a few comments regarding claim construction are needed. It appears to be common ground between appellant and the Examiner that the term therapeutically treating includes but does not require a complete cure. For example, paragraph 137 of the specification indicates that therapeutically treating includes "at least partially arresting" a disease as well as curing. Likewise, it is believed to be common ground that prophylactically treating includes but does not require complete prevention. Paragraph 137 of the specification discloses that prophylactic treatment can "eliminate, reduce the risk, less the severity or delay the onset of disease" (*see, e.g.*, specification at paragraph 137). The dictionary definitions cited by the Examiner are largely consistent with the definitions in the specification. Further, the Examiner remark that the claims "*encompass* both preventing and curing Lewy Body disease" (penultimate office action at p. 6, second paragraph, emphasis supplied) suggests the Examiner agrees that therapeutically treating and prophylactically treating include but do not require a complete cure or complete prevention. As properly construed, appellants respectfully submit that the claims are enabled.

Enabling the full scope of a claim does not necessarily require enabling every embodiment within the claim. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 414 (Fed. Cir. 1984). This principle is applied to a method of treatment by *In re Cortright,* 165 F.3d 1353, 49 USPQ2d 1464 (Fed. Cir. 1999). One of the claims at issue in *In re Cortright* was directed to a method of treating baldness. The Board had rejected the claim for lack of enablement on the basis that the specification did not show restoring the user's hair to its original state (*i.e.*, a full head of hair) but only some improved growth characterized as "filling-in some" or "fuzz" (*Id.* at 1358, 49 USPQ2d at 1467). The Federal Circuit construed the claims as meaning that the claimed method increased the amount of hair grown on the scalp but did not necessarily produce a full head of hair (*Id.* at 1359, USPQ2d at 1468). The Federal Circuit concluded that the claims, so construed, were enabled, notwithstanding the lack of evidence that complete restoration could be achieved.

The same principle is illustrated in a different technology by *CFMT, Inc. v. Yieldup Int'l Corp,* 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003). The patent at issue was directed to a method of cleaning semi-conductor wafers. The available evidence showed that the disclosed method could remove some contaminants, but could not remove all contaminants, nor even achieve removal of contaminants to a commercial standard. The Federal Circuit reversed the district court's holding of lack of enablement.

> In essence the district court set the enablement bar too high. Enablement does not require an inventor to meet lofty standards for success in the commercial marketplace. Title 35 does not require that a patent disclosure enable one of ordinary skill in the art to make and use a perfected commercially viable embodiment absent a claim limitation to that effect.
>
> In sum, any meaningful "cleaning" would satisfy the claimed goal of "cleaning of semiconductor wafers."
>
> *Id.* at . 1338-1340, 68 USPQ2d at 1944-45.

A recent unpublished decision of the USPTO Board of Patent Appeals and Interferences is instructive in applying the above Federal Circuit precedents to claims encompassing methods of treatment. *Ex parte Saito,* Appeal No. 2005-1442 (BPAI 2005, nonprecedential opinion) concerned claims directed to methods of introducing a nucleic acid into a subject by transplanting a hair follicle modified to contain the nucleic acid. The claims were rejected by the examiner for lack of enablement because, although the claims were not limited to therapeutic methods, the claims encompassed such methods, and the examiner took the view that undue experimentation would be required to achieve therapeutic levels of gene expression. The Board followed the precedent of *In re Cortright* in reversing the examiner.

> As with the present claims, the claims in *Cortright* encompassed a method of obtaining results that might be difficult to achieve: here, therapeutically effective gene therapy; in *Cortright,* complete restoration of hair growth. However, as in *Cortright,* the present claims do not require that particular result: the present claims require only introducing or delivering a nucleic acid; *Cortright's* claims required only some restoration of hair growth.

> The court in *Cortright* did not dispute the board's conclusion that completely restoring hair growth using Bag Balm® would require undue experimentation [citation omitted]. The court nonetheless concluded that the claimed method was not nonenabled merely because it encompassed one difficult-to-achieve outcome. The same reasoning applies here: the examiner may be correct that achieving clinically useful gene therapy using the claimed method would require undue experimentation, but the claims are not nonenabled merely for encompassing that difficult-to-achieve outcome.
>
> *Ex parte Saito,* Appeal No. 2005-1442, at pp. 6-7.

Here, as in *In re Cortright* or *Ex Parte Saito,* the present claims include but do not require a complete cure or complete prevention. Assuming *arguendo* that the claimed methods cannot completely cure or prevent Parkinson's disease, they would be no different than treatment or prophylaxis with many other highly successful drugs. For example, it is well known that the commercial success of certain cancer drugs is measured in increments of extending the life of a patient by few months, a result far removed from complete cure or prevention. Further, a quick search of the PTO database reveals that the Patent Office has granted thousands of patents to methods of treatment and/or prophylaxis of disease notwithstanding that it is common knowledge that few drugs achieve such lofty goals as complete cure or complete prevention. In these circumstances, Appellants submit that in the presently claimed methods, as in other patents claiming methods of treatment or prophylaxis, the possibility that the methods may not achieve a complete cure or complete prevention is not detrimental to enablement and need not be excluded from the claims.

The Examiner's remarks in the final rejection attempting to rebut appellants' position do not address the legal issue above.

> Applicant's arguments are not persuasive because applicant's invention does not teach even one circumstance claimed. There are no examples of curing or preventing and no apparent circumstances wherein any animal is cured or the entire pathology of the disease is prevented.
>
> Final office action at p. 3, second paragraph

Appellants have accepted for purposes of this discussion that the examples of the specification, although showing a reduction in alpha synuclein deposits in a model of Parkinson's disease, achieved less than a complete cure or complete prevention. What is at issue is whether a claim to a method that includes but does not require a complete cure or complete prevention requires such evidence. For the reasons given above, appellants respectfully submit that such evidence is not required, and that the rejection should be reversed.

7.2 Claims 41, 42, 44, 45, 46, 48, 50, 51-55, 71, 72, 74, 75, 76 and 80-84 Not Anticipated by Jensen, 2002 or Jensen, 2003.

7.2.1 Summary of the References

The two Jensen patent applications are substantially cumulative with one another, and will be treated as one except when citing to specific paragraphs. The Jensen applications are directed to an alleged improvement to earlier work by Schenk (one of the present inventors) in which immunization with Aβ was shown to reduce deposits of Aβ in the brain of a transgenic model of Alzheimer's disease. The work of Schenk is discussed in paragraphs 49 to 53, 252 and 253 of Jensen, 2003. One of the Schenk references referred to by Jensen at col. 4, line 53, WO 99/27944, is a corresponding application to Schenk, US 6,787,144 (#C, PTO-892, April 7, 2005). It can be seen that this patent discusses immunization with Aβ to treat Alzheimer's disease, and also mentions that other amyloid peptides responsible for other amyloidogenic diseases can likewise be used in treating the respective disease with each peptide is associated.

> The same or analogous principles determine production of therapeutic agents for treatment of other amyloidogenic diseases. In general, the agents noted above for use in treatment of Alzheimer's disease can also be used for treatment early onset Alzheimer's disease associated with Down's syndrome. In mad cow disease, prion peptide, active fragments, and analogs, and antibodies to prion peptide are used in place of Aβ peptide, active fragments, analogs and antibodies to Aβ peptide in treatment of Alzheimer's disease. In treatment of multiple myeloma, IgG light chain and analogs and antibodies thereto are used, and so forth in other diseases.
>
> US 6,787,144 at col. 12, lines 4-16

The alleged improvement of Jensen over Schenk resides in the use of modified forms of Aβ or other amyloidogenic peptides to stimulate a stronger immune response (see paragraphs 53, 55, 85, 183 and 251-260 of Jensen, 2003). The Jensen applications are mainly directed to using modified forms of Aβ for the treatment of Alzheimer's disease. However, as in the original Schenk work, Jensen also mentions others amyloidogenic diseases and corresponding peptides in which an analogous strategy can be adapted (see paragraphs 43-46 and 247).

7.2.2 The Examiner's rationale

The Examiner's rationale is set forth in the penultimate office action and final rejection. In brief, the Examiner' points to separate sections of the Jensen applications referring to Parkinson's disease or administration of Aβ peptide, and alleges that the artisan would put these together to arrive at a method of treating Parkinson's disease using Aβ peptide. Additionally, or alternatively the Examiner alleges anticipation from disclosure of using Aβ to treat or prevent genera of diseases that include Parkinson's disease within their scope.

7.2.3 The Cited Art Distinguished

In appellants' submission, the Jensen applications do not clearly disclose that Aβ peptide be administered to treat Parkinson's disease. Jensen is mainly directed to administration of Aβ for the treatment of Alzheimer's disease. Jensen also mentions other "Alzheimer-like" diseases, including Parkinson's, Huntington's and prion-related diseases (*see* paragraph 247). However, Jensen does not disclose that the very same treatment for Alzheimer's disease (namely administration of Aβ) should also be given to patients with or at known genetic risk of the other diseases mentioned including Parkinson's. In fact, Jensen does not refer to administration of Aβ and Parkinson's disease in the same sentence or even the same paragraph. Insofar as one can determine what Jensen is proposing, it would appear more likely he is proposing that amyloidogenic diseases principally associated with peptides other than Aβ be treated not with Aβ, the major peptide associated with Alzheimer's disease, but with whatever peptide plays a comparable role in the disease in question.

In the final office action, the Examiner alleges that appellant has not identified any support for appellants' proposed interpretation of Jensen. The Examiner also alleges, presumably in favor of an alternative construction of Jensen in which Jensen does disclose administration of Aβ to Parkinson's patients, that the skilled person would understand the value of using Aβ to treat Parkinson's disease in view of comments by Primavera et al., J. Alzheimer's Dis. 1, 183-193 (1999) that deposits of Aβ are found in some Alzheimer's patients.

Appellants respectfully submit that their interpretation of Jensen is in fact more consistent with Jensen's disclosure and what Jensen believes is his own contribution over the art. As discussed above, Jensen believes his contribution over earlier work by Schenk lies in providing modified forms of Aβ and other amyloidogenic peptides that induce enhanced immune responses. Most of the specification is devoted to producing modified forms of Aβ and the examples are devoted to administering modified forms of Aβ to a transgenic animal of Alzheimer's disease. The listing of alternative amyloidogenic peptides and amyloidogenic diseases can thus be understood as an indication that the strategy exemplified for Aβ (i.e., making a modified form and immunizing in a model of Alzheimer's disease) can be extended to other amyloidogenic peptides and their respective diseases. There is no reason to credit Jensen with a second insight of administering Aβ to treat Parkinson's disease when he does not exemplify such a strategy, theorize why such a strategy would work or even describe administering Aβ and treatment of Parkinson's disease in the same sentence or paragraph.

Insofar as Primavera is relied on by the Examiner to support an alternative interpretation of Jensen, appellants submit such reliance is both procedurally and substantively incorrect. Reliance is procedurally incorrect because Primavera is not included in the statement of rejection but is merely mentioned as art that is being made of record but "not relied on." Reliance on Primavera is also improper because Primavera appears to be asserted in a theory of obviousness (i.e., the skilled person would have been motivated to administer Aβ to Parkinson's patients because of Primavera's teaching that some such patients have deposits of Aβ). If it is necessary to reach beyond the boundaries of a single reference to provide missing disclosure of the claimed invention, the proper ground is not §102, anticipation but §103, obviousness. *Scripps Clinic & Research Foundation v. Genentech,* 18 USPQ2d 1001, 1010 (Fed. Cir. 1991).

Finally, the notion that Primavera does teach the skilled person the value of administering Aβ to treat Parkinson's disease is not an accurate reflection of Primavera's teaching. Primavera observes that Aβ deposits are present in Parkinson's disease (as well as some other diseases besides Alzheimer's). However, Primavera does not translate this into any plan to treat such patients. On the contrary, Primavera concludes only that further investigation is needed to "better understand the causes and consequences of this pathology" (at p. 190, second column, last paragraph). Thus, the Examiner's assertion that the artisan would understand from Primavera the value of treating Parkinson's disease with Aβ goes well beyond Primavera's teaching.

The Examiner cites several sections of Jensen for the proposition that Jensen discloses administration of Aβ to treat or prevent a genus of diseases that includes Parkinson's disease. For example, the Examiner relies particularly on a sentence in the Background saying that Parkinson's disease is an amyloid associated disease. It is not disputed that the Jensen publications so characterize Parkinson's disease. What is at issue is how they propose to treat it. This sentence in the background does not address this issue.

The Examiner also points to claims 34 and 20 of US 2002/0187157. Claim 34 is directed to a method of treating or preventing a genus of diseases characterized by amyloid deposits. Claim 20, from which claim 34 depends, specifies a Markush group of about fifty peptides, one of which is Aβ. In combination, claims 34 and 22 are directed to treating a broad genus of diseases with a Markush group of fifty or so agents. Such a genus probably includes over a thousand potential combinations of diseases and agents.

Description of genus having so many potential combinations none of which are individually described does not compensate for the ambiguities throughout the Jensen applications. Although the Jensen applications mention Aβ and Parkinson's disease separately, , they are never discussed in the same sentence or paragraph or otherwise in a way that clearly conveyed an intent to treat Parkinson's disease with Aβ. A description of broad genus is insufficient to provide written description of individual members within that genus. *In re Ruschig,* 154 USPQ 118 (CCPA 1967). "Not having been specifically named or mentioned in any manner, one is left to select from the myriads of possibilities encompassed by the broad

disclosure with no guide indicating or directing that this particular compound should be made rather than any of the many others which could also be made."

A similar analysis applies to claim 27 of US 2003/0086938 referred to by the Examiner at p. 9 of the penultimate office action . This claim is directed to a method of treating or preventing a genus of Alzheimer's disease or other disease and conditions characterized by Aβ deposits by downregulating Aβ or APP. Assuming *arguendo* that some patients with Parkinson's disease also have deposits of Aβ and thus constitute a subset of the specified genus, and that methods of downregulating Aβ include administration of Aβ, the claim still provides no specific disclosure of the combination of treating Parkinson's disease with Aβ.

To argue that a claim to a genus inherently discloses all species is "wholly meritless whether considered under section 102(b) or under 103." *Corning Glass Works v. Sumito Electric,* 9 USPQ2d 1967 (Fed. Cir. 1989). In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity" to constitute an anticipation under the statue. What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims. MPEP 2131.04. The criticality of a claimed subgenus turns on whether the claim is an advance over prior products and processes previously known and sufficiently distinctive to warrant a patent monopoly. There must be a distinctive physical, here a chemical, discovery. *California Research Lab. v. Ladd,* 148 USPQ 404, 410 (DC 1966). Here, the prior art genus is directed to treating or preventing Alzheimer's disease or other disease characterized by deposits of Aβ. Virtually anyone is potentially susceptible to Alzheimer's disease if they live long enough and could thus could be treated to prevent Alzheimer's disease. The present claims encompass only a relatively narrow species of this genus, that is, patients having or at known genetic risk of Parkinson's disease. Moreover, treatment of the claimed class of patients is associated with a result not shared by the broader genus. That is, in treatment of claimed class of patients, the agent is active not only against Aβ deposits that characterize the entire genus, but against synuclein deposits that characterize the

claimed class of patients (see specification at paragraph 186 and Figs. 5 and 6). There is nothing in the art to indicate that this result was expected before the effective filing date of the invention.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a prima facie case based upon the prior art (*In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984)). If the evidence is in "equipoise," an inventor is "entitled to a patent." *In re Oetiker,* 24 USPQ2d 1443, 1447 (Fed. Cir. 1992) (Plager, J., concurring). Here, the cited reference refers separately to Aβ and Parkinson's disease but never in the same sentence or paragraph or otherwise in a manner that clearly conveys an intent to administer Aβ for the treatment of Parkinson's disease. As discussed above, it is in fact unlikely that this was what Jensen intended. However, insofar as there is doubt on this issue, the doubt should inure to the benefit of appellants given that the burden of proof rests with the Patent Office.

The Board is also requested to consider the patentability of claims 54, 55 and 81-84 directed to methods of treatment or prophylaxis of patients free of Alzheimer's disease or patients free of clinical symptoms of amyloidogenic diseases characterized by extracellular amyloidogenic deposits. The cited Jensen applications provided no specific disclosure connecting treatment with Aβ or antibodies thereto with such patients free of Alzheimer's disease or free of clinical symptoms of diseases characterized by extracellular amyloid deposits. Although the Jensen applications might evidence an intent to treat Parkinson's patients, they do not distinguish between Parkinson's patients with or without concurrent Alzheimer's disease. Thus, the Jensen publications provide no specific disclosure of the classes of patients to which claims 54, 55 and 81-84 are directed, much less a clear intent to treat such patients with Aβ or an antibody thereto.

In the final rejection, the Examiner addresses the above position but in the context of the rejection under 35 USC 103(a) rather than in the context of 35 USC 102(e) in which the above distinctions were raised. In any event, the Examiner's position is that Jensen discloses prevention of Alzheimer's disease and that the only way to prevent Alzheimer's disease is to administer it to patients who do not have Alzheimer's disease. Presumably, the Examiner's point is that such a genus would include some patients having Parkinson's disease (as required by

claims 41 and 44) and some patients at known genetic risk of Parkinson's diseases (as required by claims 71 and 74). This position raises a similar issue to that previously discussed. Disclosure of a genus does not necessarily anticipate or render obvious a species when that species is not specifically enumerated by the reference, particularly when that the species is a relatively small part of the genus disclosed in the reference and associated with an unexpected result. Here, the genus of the cited art is large in that virtually anyone who does not have Alzheimer's disease could be treated to prevent Alzheimer's disease from developing in the future. The claims at issue encompass only a narrow species of that genus, namely patients having Parkinson's disease or a known genetic risk thereof. Moreover, this species is associated with an unexpected result: immunization with Aβ reduces alpha synuclein deposits even in the absence of abnormal Aβ deposits (specification at paragraph 186 and Figs. 5 and 6). Although Aβ has been previously shown to reduce deposits of Aβ (see, e.g., US 6,787,144), there was no reason to expect it would reduce the deposits of a different protein alpha synuclein particularly in patients lacking abnormal deposits of Aβ. Because claims 54, 55 and 81-84 encompass only a small species of the prior art genus of subjects not already having Alzheimer's or other amyloidogenic disease who can be subject to prophylaxis for Alzheimer's disease, and this species is associated with an unexpected result, the present claims are not anticipated or rendered obvious by the Jensen applications.

Claims 44 and 74 are further distinguished in that the Jensen applications do not provide specific disclosure of methods in which a combination of Aβ or antibody thereto and alpha synuclein or an antibody thereto is administered. Although the Jensen publications may generally refer to using at least one amyloidogenic polypeptide or subsequence thereof, the publications list many examples of such polypeptides, and do not disclose the specific combination of Aβ and alpha synuclein. The Examiner has not addressed these distinctions to date.

7.3 Claims 41, 43-46, 48, 50-55, 71, 73-76, 78-80 and 80-84 Not Obvious Over Jensen, 2002 or Jensen, 2003

The rejection was originally applied on the basis that Jensen teaches all elements of the above claims except the administration of antibodies instead of immunogenic peptides.

The Examiner took the view that administration of antibodies would have been obvious in view of the goal of vaccination with peptides being to generate antibodies (penultimate office action at p. 10, last paragraph). In reply, appellants disagree that Jensen teaches all elements of the above claims except the administration of antibodies, for the reasons discussed in connection with the anticipation rejection. Thus, the further issue of disclosure of antibodies is moot.

In the final office action, the Examiner does not further address the issue of disclosure of antibodies but instead refers to appellants' remark on the separate patentability of claims 54, 55 and 81-84 which were made with respect to the rejection under 35 USC 102(e). The tenor of the Examiner's remarks ("Jensen clearly contemplates the limitations of said claims," final office action at p. 4, second paragraph) suggests that the Examiner's remarks were in reference to the rejection under 35 USC 102(e) rather than a new ground of obviousness rejection. Thus, these remarks have been addressed above, and appellants do not further address them here.

8. CONCLUSION

For these reasons, it is respectfully submitted that the rejection should be reversed.

Respectfully submitted,

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9. CLAIMS APPENDIX

41. A method of therapeutically treating a patient suffering from Parkinson's disease, the method comprising

administering to the patient an effective regime of an agent that induces an immunogenic response against Aβ in the patient and thereby therapeutically treating the disease;

wherein the agent is Aβ or an immunogenic fragment thereof, or is an antibody to Aβ.

42. The method of claim 41, wherein the agent is Aβ or an immunogenic fragment thereof.

43. The method of claim 41, wherein the agent is an antibody to Aβ.

44. A method of therapeutically treating a patient suffering from Parkinson's disease, comprising

administering to the patient an effective regime of an agent that induces an immunogenic response against alpha-synuclein and an agent that induces an immunogenic response against Aβ in the patient and thereby therapeutically treating the disease;

wherein the agent that induces an immunogenic response against alpha-synuclein is alpha synuclein or an immunogenic fragment thereof or an antibody to alpha synuclein, and the agent that induces an immunogenic response against Aβ is Aβ or an immunogenic fragment thereof, or an antibody to Aβ.

45. The method of claim 41, wherein the agent is administered peripherally.

46. The method of claim 41, wherein the effective regime comprises administering multiple dosages over a period of at least six months.

48. The method of claim 41, wherein the patient has a risk factor for the disease.

51. The method of claim 41, wherein the administering results in improvement in a sign or symptom of Parkinson's disease.

52. The method of claim 41, wherein the administering improves motor characteristics of the patient.

53. The method of claim 41, further comprising monitoring a sign or symptom of Parkinson's disease in the patient.

54. The method of claim 41, wherein the patient is free of Alzheimer's disease.

55. The method of claim 54, wherein the patient is free of Alzheimer's disease and has no risk factors thereof.

71. A method of prophylactically treating a patient having a known genetic risk of Parkinson's disease, the method comprising

administering to the patient an effective regime of an agent that induces an immunogenic response against Aβ in the patient and thereby effecting prophylaxis of the disease;

wherein the agent is Aβ or an immunogenic fragment thereof, or is an antibody to Aβ.

72. The method of claim 71, wherein the agent is Aβ or an immunogenic fragment thereof.

73. The method of claim 71, wherein the agent is an antibody to Aβ.

74. A method of prophylactically treating a patient having a known genetic risk of Parkinson's disease in the brain, comprising

administering to the patient an effective regime of an agent that induces an immunogenic response against alpha-synuclein and an agent that induces an immunogenic response against Aβ in the patient and thereby effecting prophylaxis of the disease;

wherein the agent that induces an immunogenic response against alpha-synuclein is alpha synuclein or an immunogenic fragment thereof or an antibody to alpha synuclein, and the agent that induces an immunogenic response against Aβ is Aβ or an immunogenic fragment thereof, or an antibody to Aβ.

75. The method of claim 71, wherein the agent is administered peripherally.

76. The method of claim 71, wherein the effective regime comprises administering multiple dosages over a period of at least six months.

79. The method of claim 71, wherein the patient is free of Alzheimer's disease.

80. The method of claim 79, wherein the patient is free of Alzheimer's disease and has no risk factors thereof.

81. The method of claim 41, wherein the patient is free of clinical symptoms of a disease characterized by extracellular amyloid deposits.

82. The method of claim 45, wherein the patient is free of clinical symptoms of a disease characterized by extracellular amyloid deposits.

83. The method of claim 71, wherein the patient is free of clinical symptoms of a disease characterized by extracellular amyloid deposits.

84. The method of claim 74, wherein the patient is free of clinical symptoms of a disease characterized by extracellular amyloid deposits.

10. EVIDENCE APPENDIX

US 6,787,144 (reference #C cited by Examiner on PTO-892, April 7, 2005).

11. RELATED PROCEEDINGS APPENDIX

Appeals are also pending in related Application Nos. 09/723,765 and 10/923,471. No Board or court decision has issued in these cases.